REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claim Amendments

The route of administration has been limited to oral administration, based upon paragraph [0025] on page 10 of the specification.

Claim 6 has been amended to recite "to the oral administration of the insulin resistance-improving agent", based upon (at least) paragraph [0032] of the specification. Similarly, claim 25 has been amended to recite "to the oral administration of the pharmaceutically acceptable anion exchange resin".

The diseases in claims 15-18 have been limited to hyperinsulinism, renal dysfunction, and fatty liver.

Claims 4, 8 to 14, 19, 20, and 23 have been cancelled, without prejudice or disclaimer.

New claims 27 to 35 are added. Support for the term "prophylactic treatment" in the new claims can be found in paragraph [0034] of the specification, and the results of Example 1.

Claim of Priority

The Examiner has failed to acknowledge the claim for foreign priority or receipt of the foreign priority document. The claim for foreign priority is set forth in the Declaration. Additionally, the Notice of Acceptance mailed June 6, 2007 indicates that the priority documents were received by the PTO. Also, the Image File Wrapper for this application includes the certified copy of the foreign priority application.

Accordingly, the Examiner is respectfully requested to acknowledge the claim for foreign priority and receipt of the priority document with the next correspondence.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-26 are rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification, while enabling for improving insulin resistance by oral administration, does not provide enablement for improving insulin resistance by any route of administration. This rejection is rendered moot in view of the claim amendments.

Claims 15-26 are rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification, while enabling for improving and treating a disease or symptom resulting from insulin resistance, does not reasonably provide enablement for prophylaxis of a disease or symptom resulting from insulin resistance. This rejection is respectfully traversed.

Applicants assert that both "prophylaxis" (claim 15) and "prophylactic treatment" (new claim 27) are enabled by the teachings of the specification.

Specifically, the experimental results set forth in Example 1 of the specification demonstrate improvement of insulin resistance by colestimide in the prophylactic treatment group. Please see Example 1, parts (4), (5) and (6) on page 16 of the specification.

As explained in "1. Test method" on page 14 of the specification, 45 ApoE3 Leiden mice were fed with a high fat diet (45.4% fat) for 3 weeks, and then divided into two groups. The first group (30 mice) was continued on the high fat diet, and the second group (15 mice) was fed the high fat diet containing 1.5% (w/w) colestimide, for 12 weeks. This latter group was deemed the colestimide prophylactic treatment group.

At the start of the administration, no differences were observed between the control group and the treatment group in body weight (Fig. 1), feed intake (Fig. 2), plasma sugar level (Fig. 4), and plasma insulin level (Fig. 5), and the values were found to be normal in both of the groups. Accordingly, it was confirmed that the test animals in both of the groups (control and colestimide prophylactic treatment group) were not in any pathological condition.

During the course of the experiments, the values were more significantly changed with the passage of time in the control group to create worse pathological conditions, while in the prophylactic treatment group, improvement in insulin resistance was observed after 20 weeks. Please see Fig. 6: Example 1, part (5) and Fig. 7: Example 1, part (6).

Thus, the experimental results set forth in Example 1 demonstrated prophylaxis and prophylactic treatment of insulin resistance by colestimide in the test animals. Specifically, the animals in the colestimide prophylactic treatment group did not develop insulin resistance, and thus providing enablement for the "prophylaxis" (i.e., prophylactic treatment) of a disease or symptom resulting from insulin resistance," as claimed.

In view of the comments provided above, it is respectfully asserted that the present claims are enabled in their present form, and the rejection should accordingly be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 4, 6, 7, 13, 14, 23, 25 and 26 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite. This rejection is respectfully traversed.

With regard to the term "derivative", claims 4, 11 and 23 have been cancelled. In claims 7 and 26, Applicants assert that the meaning of "derivative" is clear, based upon the teachings of the specification, and the knowledge of those skilled in the art. MPEP 2173.02 states, "[d]efiniteness of claim language must be analyzed, not in a vacuum, but in light of: (A) [t]he content of the particular application disclosure; (B) [t]he teachings of the prior art; and (C) [t]he claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

Claims 7 and 26 recite "pharmaceutical preparations comprising GLP-1 or derivatives thereof", wherein the term "pharmaceutical preparations" recited in these claims clearly refers to an example of a "hypoglycemic agent". Accordingly, the scope of GLP-1 having hypoglycemic action, or derivatives thereof, would be readily understood by one of ordinary skill in the art. Specifically, a GLP-1 derivative would be understood by one of ordinary skill in the art to mean a "GLP-1 analogue" as a glucagon-like peptide-1 (GLP-1) receptor agonists. For reference, Applicants enclose herewith an article from "Diabetes, Obesity and Metabolism" (Attachment 1), in which the term "GLP-1 derivatives" is considered to have the same meaning as "GLP-1 analog". Thus, the term "derivatives" as set forth in the present claims is not indefinite.

With regard to the phrase "of which typical example includes", claims 4, 11 and 23 have been cancelled.

With regard to the phrase "is used simultaneously, separately, or successively", the claims have been amended in line with the Examiner's suggestion.

In view of the above comments and amendments, it is respectfully requested that the indefiniteness rejection be withdrawn.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-26 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 2003/011308. The Examiner relies upon US 2004/0191209 as the English language equivalent.

Claims 1-3, 6-10, 13-22, 25 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Garg (Cholestyramine Therapy for Dyslipidemia in Non-Insulin-dependent Diabetes Mellitus).

These rejections are respectfully traversed.

The Examiner takes the position that WO '308 discloses that administration of colestimide inhibited blood sugar elevation after eating in patients with hypercholesterolemia complicated by type 2 diabetes. The Examiner also takes the position that Garg discloses that it is possible to lower cholesterol and control diabetes by administration of cholestyramine.

However, WO '308 is directed to a method of inhibiting a postcibal increase in blood glucose level, i.e., **improving hyperglycemia after a meal**, and Garg discloses that a specific anion exchange resin improves glucose level in **non-insulin dependent diabetes mellitus**. The references fail to teach or suggest the administration of an anion exchange resin for **improving insulin resistance to a patient in need thereof**.

Further, the references fail to teach or suggest that an anion exchange resin is effective for prophylactic, improving, and or therapeutic treatment of hyperinsulinism, renal dysfunction, and fatty liver resulting from insulin resistance. Independent claims 15 and 27 define the disease or symptom resulting from insulin resistance as hyperinsulinism, renal dysfunction, or fatty liver.

In the present case, WO '308 and Garg each clearly fail to teach or suggest the oral administration of a pharmaceutically acceptable anion exchange resin to a patient in need of prophylaxis, improvement or treatment of hyperinsulinism, renal dysfunction, or fatty liver.

In order to anticipate a claim, it is necessary that each and every element of the claim be described, either expressly or inherently, in a single prior art reference. Therefore, neither WO '308 nor Garg anticipate the limitations of Applicants' claims.

Furthermore, these references disclose that a specific anion exchange resin reduces a serum blood level. However, one of ordinary skill in the art would not have understood that a compound having decreasing action on blood glucose level necessarily has improving action on insulin resistance. For example, sulfonylurea drugs, which are widely and commonly used as medicaments for the treatment of diabetes, do not have any effect on insulin resistance, although they have a reducing action on blood glucose level by stimulating insulin secretion. Moreover, it is reported that sulfonylureas may sometimes aggravate insulin resistance as a result of induced high secretion of insulin. Please see Box 1 on page 122 of the enclosed article from "*Cardiol. Clin.*" (Attachment 2). Accordingly, a compound which has a decreasing action on blood glucose level does not necessarily have improving action on insulin resistance. Thus, the methods of Applicants' claims are not obvious over the teachings of the cited references.

For the above reasons, it is respectfully requested that the rejections based on WO '308 and Garg be withdrawn.

Claims 1-26 are also rejected under 35 U.S.C. § 102(b) as being anticipated by JP 2002-537390.

This rejection is respectfully traversed.

The Examiner takes the position that JP '390 disclose that a hypoglycemic agent can be used to treat insulin resistance either by itself, or in combination with cholestyramine or colestipol.

However, JP '390 fails to teach or suggest that an **anion exchange resin** is effective for **improvement of insulin resistance**, and fails to teach or suggest that an anion exchange resin is effective for prophylactic, improving, and or therapeutic treatment of hyperinsulinism, renal dysfunction, and fatty liver resulting from insulin resistance.

JP '390 discloses that a class of disclosed compounds (hypoglycemic agents) has an improving effect on serum glucose level, and the reference also suggests the combination use of the disclosed compounds with cholestyramine or colestipol. However, the reference is completely silent regarding the improvement of insulin resistance by administration of a pharmaceutically acceptable anion exchange resin. On the contrary, cholestyramine and colestipol are disclosed in the reference as examples of a therapeutic agent for the treatment of hypolipidemia/hypolipoproteinemia.

Further, the reference fails to teach or suggest that an anion exchange resin is effective for prophylactic, improving, and or therapeutic treatment of hyperinsulinism, renal dysfunction, and fatty liver resulting from insulin resistance, as required by independent claims 15 and 27.

Accordingly, the subject matter of Applicants' claims is also patentable over the JP '390 reference, and withdrawal of the rejection is respectfully requested.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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ATTACHMENTS: (1) Dong, J. Z., et al., "Discovery and characterization of taspoglutide, a novel analogue of human glucagon-like peptide-1, engineered for sustained therapeutic activity in type 2 diabetes", *Diabetes, Obesity and Metabolism*, 13, 2011, pp 19-25.

(2) Jawa, Ali A., et al., "Role of Insulin Secretagogues and Insulin Sensitizing Agents in the Prevention of Cardiovascular Disease in Patients who have Diabetes", *Cardiology Clinics*, 23, 2005, pp 119-138.